

Special Article - Malnutrition

Role of Zinc in Malnutrition

Mittal P* and Dipti B

Department of Paediatrics, Govt Medical College & Rajindra Hospital, India

*Corresponding author: Mittal Parveen, Department of Pediatrics, Govt Medical College & Rajindra Hospital, 37, Khalsa College Colony, Patiala 147001, India

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Abstract

Malnutrition is a globally prevalent disease, more so in the developing countries. It includes both macronutrient and micronutrient or trace element deficiency. Of late, zinc has been recognized as an essential trace element, required for maintaining normal body homeostasis. Zinc deficiency is associated with growth retardation (height and weight), delayed sexual and bone maturation, impaired immune function, recurrent infections, dermatitis, diarrhoea, alopecia, anorexia and mental disturbances. Serum zinc levels have been found to be low in protein energy malnutrition globally. Zinc supplementation during the rehabilitation phase of malnutrition has been associated with rapid weight gain.

Keywords: Malnutrition; Protein energy malnutrition; Zinc supplementation; Zinc deficiency

Abbreviations

WHO: World Health Organisation; UNICEF: United Nations International Children's Emergency Fund, PEM: Protein Energy Malnutrition.

Introduction

Malnutrition is defined by WHO (World Health Organization) as "the cellular imbalance between the supply of nutrients and energy and the body's demand for them to ensure growth, maintenance, and specific functions". It not only includes deficiency of calories and proteins, but also micronutrient deficiency [1].

Micronutrients are the nutrients required by organisms throughout life in small quantities to perform a range of physiological functions [2]. They do not serve as energy stores but are important in cellular metabolism and are related to enzyme systems where they act either as cofactors for metal ion activated enzymes or as specific constituents of metallo-enzymes, bodily functions and in protection of the body against oxidative damage. The various micronutrients include Vitamin A, iodine, iron, zinc, calcium, vitamin D, vitamin B complex and vitamin C.

Among all micronutrients, zinc is the latest and upcoming one, having various roles in the body. Of late, it has been proven to have a very important role in growth and development, its deficiency leading to growth retardation and various other problems. Despite a large amount of zinc present in some tissues (maximum in prostate, followed by bones, liver, muscle, kidney and then by adrenals, brain, testes, spleen and lung) zinc exchange between them is limited and supply of zinc for tissue growth and repair is dependent on continuous external supply [3].

Objectives

To compile the past and present information about the role of zinc in malnutrition.

Methods

The methodology involved review of articles retrieved on Google Scholar, Pubmed, Medline, Cochrane database and Medscape (

using "role of zinc", "zinc deficiency" "zinc in malnutrition" "zinc supplementation"), restricted to English language.

Recommended dietary allowance, absorption and sources of zinc

Recommended dietary allowance: Refer Table 1 below [4].

Best dietary sources: Lean red meat is the best source. Whole-grain cereals (milling reduces their zinc concentration), legumes and pulses are also good sources [5]. Colostrum contains 3-4 times more zinc than true milk, [6] probably due to the preparturient cortisol surge [7]. Though human milk contains less zinc than cow's milk, its bioavailability is more compared to the latter [8].

Enhancers of zinc absorption: Animal proteins are the most effective type of proteins in improving zinc absorption. Some legume-based diets (eg. White beans, lupin proteins are almost as effective as animal proteins in improving zinc absorption. Approximately, twice the amount of zinc is absorbed from a high meat diet compared to a diet based on rice and wheat flour. Absorption is also facilitated by digestible dietary proteins, histidine, cysteine, citrate, picolinate and EDTA [9-11].

Inhibitors of zinc absorption: Phytates (in whole grain cereals and legumes) bind zinc, making it unavailable for absorption. Other dietary minerals such as iron, calcium and copper also interfere with zinc absorption [12-14].

Methods to improve zinc absorption: Methods to improve zinc absorption include 1. Reducing phytate intake by A. Using germinated cereals and legumes. B. Use fermentation (yeast) in dough for making bread. 2. Include sources of animal protein (meats and fish are the best, but milks also improve the bioavailability). 3. Use infant formula, made from whey-adjusted cow's milk rather than from formula made from phytate-rich vegetable proteins such as soy [5].

Importance of Zinc in Nutrition

Zinc is known since long as Indian Ayurvedic physicians (5000 B.C.) used to prescribe it in the form of snuff to bring patients out of coma [15]. The use of zinc oxide in calamine has been mentioned in

Table 1: Recommended dietary allowance of zinc.

AGE	MALE	FEMALE	PREGNANCY	LACTATION
0-6 month	2 mg	2 mg	-	-
7-12 month	3 mg	3 mg	-	-
1-3 years	3 mg	3 mg	-	-
4-8 years	5 mg	5 mg	-	-
9-13 years	8 mg	8 mg	-	-
14-18 years	11 mg	9 mg	12 mg	13 mg
19 years & above	11 mg	8 mg	11 mg	12 mg

Ebers Papyrus of 1550 B.C. The biological importance of zinc was first discovered by Raulin in 1869, which showed that it was essential for the growth of *Aspergillus Niger* [16]. It was also shown to be essential for the growth of higher plants [17,18]. In 1939, beri-beri patients in China were noted to have decreased zinc levels in skin and nails. In 1950, a normal serum zinc level was 1st defined, and found to be 17.3-22.1 $\mu\text{mol/L}$. In 1956, cirrhotic patients were found to have low serum zinc levels.

The first case of human zinc deficiency was described in early 1961 by Prasad et al., who described a syndrome of zinc deficiency characterized by dwarfism, anaemia, rough skin, hepatosplenomegaly, mental lethargy and geophagia [19]. In 1974, the National Academy of Sciences declared zinc to be an essential element for humans and established a recommended daily allowance. In 1978, the Food and Drug Administration required zinc to be in total parenteral nutrition. In the 1990's, there was an increasing attention on the role of zinc deficiency in childhood morbidity and mortality in developing countries [20]. By 2014, over 300 zinc-containing enzymes have been identified along with over 1000 zinc-containing transcription factors.

Role of Zinc in Malnutrition

Physiology

The actions of zinc include 1. Action on taste and smell acuity, appetite regulation and food consumption and regulation. 2. Action on DNA and RNA synthesis stimulating A. Cell replication and differentiation of chondrocytes, osteoblasts and fibroblasts. B. Cell transcription culminating in the synthesis of somatomedin C (liver), alkaline phosphatase, collagen and osteocalcin (bone) and C. Protein, carbohydrate and lipid metabolism, that is intimately related to the mechanisms of smell, taste, appetite and food consumption and utilisation. 3. Action on hormonal mediation by participating in A. Growth hormone synthesis and secretion B. Action of growth hormone on hepatic somatmedin C production C. Somatomedin C activation in bone cartilage. In addition, it also interacts with other hormones related to bone growth like testosterone, thyroid hormones, insulin and vitamin D3. In zinc deficiency, this homeostasis is impaired, causing the weight-height deficiency in human beings [21]. It is the cause of stunted growth in 1/3 of the world population [22].

It enhances cellular growth and differentiation. Although the exact mechanism is not known, research indicates that zinc availability affects cell-signalling systems that coordinate the response to the growth-regulating hormone, insulin-like growth factor-1 (IGF-1). Zinc deficiency may therefore limit the rate of weight gain during periods of recovery of body mass and may also determine

the composition of tissue laid down causing increased synthesis of adipose tissue rather than muscle in children recovering from malnutrition.

Zinc inhibits GSK-3 β , thus increasing glycogen synthesis. It may positively influence insulin signalling via preventing a negative regulator (GSK3 β) from suppressing insulin signalling. It stimulates leptin production and its secretion from adipocytes. Oral zinc appears to stimulate the vagal nerve which then increase mRNA translation of the two appetite stimulating neural factors orexin and neuropeptide Y (also abolished by antagonists of these receptors) [23]. Zinc activates the GPR39 receptor (a Ghrelin receptor) and since ghrelin is known to stimulate these two neural factors via the vagus nerve, it is thought that this receptor is the molecular target of zinc [24].

Serum zinc levels in PEM

We conducted a study in 1995, which suggested the mean serum zinc levels varied inversely to the severity of PEM, and showed a graded decrease from PEM grade I (103 $\mu\text{g/dl}$) to grade IV (58 $\mu\text{g/dL}$).

SP Singla conducted a study among Indian children in 1996 and found serum zinc levels to be significantly low in grade III/IV malnutrition [25].

A study conducted by B Gautam in 2008 showed that the serum zinc levels in Bangladeshi children having PEM (59.85 \pm 11.18 $\mu\text{g/dL}$), marasmus (66.73 \pm 8.23 $\mu\text{g/dL}$), kwashiorkor (49.69 \pm 10.35 $\mu\text{g/dL}$) and marasmic kwashiorkor (60.63 \pm 85.62 \pm 8.68) were significantly lower than in control group (135.88 \pm 11.88 $\mu\text{g/dL}$) [26].

In 2012, M Khare, Mohanty C et al studied the serum micro-mineral levels in children living in Eastern Uttar Pradesh, India and found low levels of zinc in the children having PEM [27].

A 2013 study done in Gujarat, India, by Asha K, Hirens S et al in preschool children with PEM showed lower serum zinc levels i.e 102.85 \pm 19.45 $\mu\text{g/dL}$ in marasmus, 109.23 \pm 22.12 $\mu\text{g/dL}$ and 99.5 \pm 15.33 $\mu\text{g/dL}$ in marasmic kwashiorkor, compared to the control group (128.5 \pm 18.32 $\mu\text{g/dL}$) [28].

Estimation of serum zinc levels in Sudanese children suffering from PEM by Elsadig Hassan et al in 2014 also revealed low values compared to the controls [29].

Lower serum zinc levels were associated with PEM with oedema (kwashiorkor) than PEM without oedema (marasmus). This signifies the importance of proper replacement of zinc as part of management of malnutrition and also during disease process.

Zinc supplementation

Despite a large amount of zinc present in some tissues (maximum in prostate, followed by bones, liver, muscle, kidney and then by adrenals, brain, testes, spleen and lung) zinc exchange between them is limited and supply of zinc for tissue growth and repair is dependent on continuous external supply [3].

Zinc supplementation during nutritional rehabilitation of mild to moderate protein energy malnutrition (PEM) hastens the recovery and ensures adequate cell growth and improves cellular immunity [30]. An adequate zinc intake during rehabilitation from severe malnutrition is essential to match the demands of rapid growth [31].

It has a positive effect on plasma zinc level, weight gain and infant morbidity [32]. Topical paste and oral zinc heals skin ulcers in kwashiorkor. Cytotoxic effects and chromosomal damage observed in children suffering from PEM can be repaired in-vitro with zinc sulphate supplementation [33]. The use of zinc in the treatment of anorexia has been advocated since 1979 by Bakan. At least 15 clinical trials have been shown to improve weight gain in anorexia. A 1994 trial showed that zinc doubled the rate of body mass increase in the treatment of anorexia nervosa [34]. A range of supplementation doses have been assessed, from 15mg-140mg/week, with the upper range exceeding the recommended daily intake for children of 2mg/day for children less than 1 year of age and up to 7mg/day for children between 1-3 years [35]. In children below 2 years, it enhances linear growth and reduces the incidence of anaemia at the dose of 10-20 mg/day, [36-39] with the stunted children benefiting more than the non-stunted children [38-40]. The beneficial effects of zinc supplementation have been most clearly demonstrated in South Asian children, when they were given at least 70mg of zinc per week [41]. Caution must be observed while selecting the dose, as high doses may cause increased mortality and morbidity [42,43].

Conclusion

Zinc is an essential nutrient for human health, and every human needs zinc to survive. Ensuring adequate levels of zinc intake is a key component in the effort to reduce child illness, enhance physical growth and decrease mortality in developing countries.

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